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Post-Vaccination Myasthenia Gravis and Vaquez Disease

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Abstract

We report the case of a 68-year-old patient who developed autoimmune myasthenia 24 hours after receiving the second dose of an inactivated SARS-CoV-2 vaccine (Sinopharm®). This patient, already followed for ischemic heart disease, presented with typical symptoms such as diplopia, bilateral ptosis, and muscle fatigability upon exertion. Investigations revealed the presence of anti-acetylcholine receptor antibodies as well as polycythemia, confirmed by the JAK2 V617F mutation, suggesting an association with a myeloproliferative disorder.

Keywords

SARS-CoV2, Myasthenia, JAK2

1. Introduction

New onset of autoimmune diseases with systemic, haematological, rheumatological and neurological manifestations are now well-recognised following SARS-CoV-2 infection. Vaccination against SARS-CoV-2 has significantly reduced the morbidity and mortality associated with the pandemic. However, adverse events, particularly autoimmune reactions, have been reported on rare occasions. Further research into possible immunological mechanisms behind this phenomenon, including identifying potential epitopes inducing molecular mimicry, could help establish possible causative links. We report the case of a 68-year-old patient with ischemic heart disease who developed autoimmune myasthenia 24 hours after receiving the second dose of the inactivated Sinopharm vaccine. The association with polycythemia vera, confirmed by the JAK2 V617F mutation, makes this case

particularly interesting and underscores the importance of post-vaccination monitoring, especially in patients with comorbidities.

2. Observation

We report the case of a 68-year-old patient with a 3-year history of ischemic heart disease, treated with bisoprolol 5 mg/day, ramipril 5 mg/day, aspirin 100 mg/day, and rosuvastatin 20 mg/day. He had never previously undergone genetic testing and had no other notable antecedents. About 24 hours after receiving a second dose of an inactivated SARS-CoV-2 vaccine (Sinopharm®), he developed diplopia associated with bilateral ptosis. These symptoms were accompanied by fatigability on exertion that resolved with rest. Additional symptoms included helmet-like headaches (a sensation of heaviness), moderate in intensity (4/10 on the numeric scale), intermittent and partly relieved by paracetamol; intermittent postural vertigo without tinnitus; and intermittent erythromelalgia in the hands and feet for about three months. On admission, he presented with a myasthenic syndrome characterized by bilateral ptosis, bilateral diplopia, partial ophthalmoplegia, and swallowing difficulties, with a myasthenic score of 75. The electroneuromyography (ENMG) did not show any decrement in the explored nerve-muscle pairs. Anti-Rach antibodies were positive at 5.1 nmol/L (normal < 0.2). A complete blood count revealed true polycythemia (hemoglobin at 19 g/dL and hematocrit at 61%). Serum electrolytes, renal function, liver function tests, protein electrophoresis, CPK, angiotensin-converting enzyme, thyroid function tests, and beta-2 microglobulin were all within normal ranges. Arterial blood gas analysis showed pH: 7.47, $PaCO_2$: 32.7 mm Hg, PaO_2: 74.7 mm Hg, SaO_2: 93.5%. The ECG revealed a regular tachycardia, and cardiac ultrasound showed only moderate left atrial dilation. A thoracoabdominopelvic CT scan was unremarkable. Testing for the JAK2 V617F mutation was positive, with an allelic frequency of 16.31%. A treatment based on pyridostigmine (4 doses of 60 mg each), prednisone (70 mg per day) and azathioprine (100 mg per day) was instituted. Good progress was noted, with disappearance of bulbar and ophthalmic signs. For Vaquez disease, bloodletting is carried out at regular intervals.

3. Discussion

We report a case of autoimmune myasthenia secondary to COVID-19 vaccination, associated with polycythemia vera (Vaquez's disease). Autoimmune myasthenia is characterized by the presence of antibodies directed against the neuromuscular junction (NMJ) [1] [2]. Viruses are recognized as environmental factors that can trigger autoimmunity in genetically predisposed individuals [3]. The mechanisms involved include both innate and adaptive immunity, particularly molecular mimicry between viral proteins and those found in peripheral nerves [4] [5]. Some vaccines (influenza, hepatitis B, human papillomavirus [HPV], and Bacillus Calmette-Guérin [BCG]) have also been implicated in autoimmune myasthenia [4]. Vadala *et al.* [6] reported that autoimmune reactions following vac-

cination likely represent fewer than 0.01% of all vaccinations, although the data may be underreported. Since the introduction of SARS-CoV-2 vaccines, numerous neurological adverse events have been described, including Guillain-Barré syndrome (GBS), cerebral venous thrombosis, peripheral facial paralysis, and transverse myelitis [7].

There are several proposed mechanisms that could explain how vaccines trigger or exacerbate an underlying autoimmune disorder like MG, including molecular mimicry between vaccine antigens and the AChR resulting in the production of cross-reactive antibodies, a potential bystander effect from inadvertent autoreactive T cell activation, epitope spreading with vaccination-induced immune response resulting in inflammatory cascades, and activation of the toll-like receptor pathway [4].

The onset of autoimmune myasthenia after SARS-CoV vaccination is very rare. To date, about twenty cases have been reported in the literature [1] [2] [4] [8]-[15]. mRNA vaccines (Pfizer-BioNTech) are most commonly implicated [4]. Inactivated virus vaccines have rarely been reported to cause autoimmune myasthenia. To our knowledge, this is only the second described case of myasthenia following the second dose of the Sinopharm vaccine (an inactivated vaccine) [8].

Repeated vaccination appears to be a triggering factor. Indeed, our patient developed ocular symptoms after the second dose of Sinopharm. This is consistent with Ramdas *et al.* [4], who found that 50% of their patients developed symptoms following the second or third vaccine dose [4].

Another distinctive feature of this case is the association of myasthenia with polycythemia vera. This combination is rare and seems to be a chance finding. In a review by Sassi *et al.* [16], only two such cases were described, one with anti-MuSK antibodies and the other with anti-Rach antibodies. Although the association between myasthenia and myeloproliferative syndromes is increasingly reported, there is no clearly established pathophysiological link at this time [17]. These authors therefore suggest that the coexistence of these two conditions is purely coincidental.

4. Conclusion

This case highlights the rarity of post-vaccination autoimmune reactions, particularly with inactivated vaccines. However, no link has been established between myasthenia and Vaquez's disease in particular and vaccination and myeloproliferative syndromes in general.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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